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Chapter 80: Contraception

INTRODUCTION

- *Contraception* prevents pregnancy by blocking sperm from reaching an ovum or stopping a fertilized ovum from implanting in the endometrium.
- While cis-women primarily use hormonal contraception, it is also used by transgender individuals, and this chapter reflects that usage.

TREATMENT

- Goal of Treatment: The prevention of pregnancy from intercourse and prevention of sexually transmitted infections (STIs) and menstrual cycle regulation.

NONPHARMACOLOGIC THERAPY

- A comparison of methods of nonhormonal contraception is provided in **Table 80-1**.
- The fertility awareness method involves avoiding intercourse when conception is likely and is linked to relatively high pregnancy rates.
- **Diaphragms** and the **cervical cap** are effective barriers used with spermicide, inserted up to 6 hours before intercourse, and left for at least 6 hours after. A diaphragm should not remain for more than 24 hours and a cervical cap no longer than 48 hours to avoid toxic shock syndrome (TTS). They do not protect against STIs, including human immunodeficiency virus (HIV).
- Most **external condoms** are latex and virus-impermeable. Some, made from lamb intestine, are not virus-proof. Water-soluble lubricants like Astroglide and K-Y Jelly prevent condom breakdown. Condoms with spermicides are not recommended as they add no extra pregnancy or STI protection and may increase HIV vulnerability.
- The **internal condom** covers the labia and cervix. It has a higher pregnancy rate than external condoms but protects against many viruses, including HIV. Do not use internal and external condoms together.
- Most spermicides contain **nonoxynol-9**, a surfactant that destroys sperm cell walls and blocks entry into the cervical os. They don't protect against STIs, and using nonoxynol-9 more than twice daily may increase HIV transmission.
- **Phexxi** is a prescription spermicide free of nonoxynol-9. It should be applied within an hour before intercourse. It lowers vaginal pH to reduce sperm motility but may cause cystitis.
- The **vaginal contraceptive sponge** contains nonoxynol-9 and offers 24 hours of protection. Leave it in place for 6 to 24–30 hours after intercourse to avoid TSS risk. It should not be reused after removal.

TABLE 80-1

Comparison of Methods of Nonhormonal Contraception

Method	Contraindications	Advantages	Disadvantages	Pregnancy Risk with Use[a]
Perfect Use	Typical Use			

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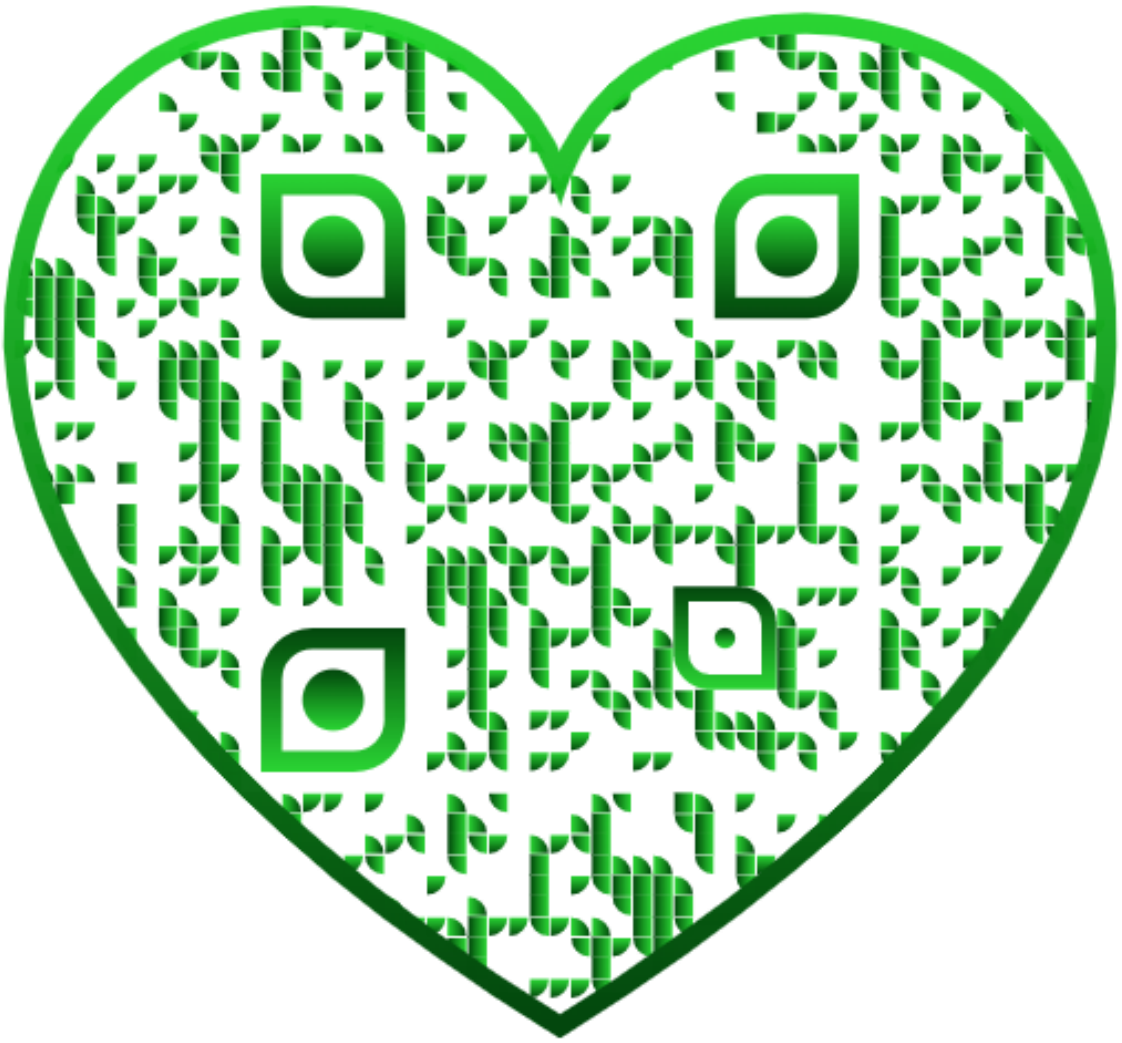

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Condoms, external (traditionally known as male)	Allergy to latex or rubber (if using latex brands); allergy to polyurethane (if using polyurethane brands)	STI protection, including HIV (latex and polyurethane only)	High failure rate Possibility of breakage Latex efficacy decreased by oil-based lubricants Possible latex allergies in either partner	2	13
Condoms, internal (traditionally known as female)	Allergy to polyurethane History of TSS	Inserted just before intercourse or ahead of time STI protection, including HIV	High failure rate May dislike ring hanging outside vagina	5	21
Diaphragm with spermicide (Caya)	Allergy to latex, rubber, or spermicide Recurrent UTIs History of TSS Abnormal gynecologic anatomy	Possible decreased incidence of cervical neoplasia Caya reusable for up to 2 years	High failure rate Proper placement required for efficacy Cervical irritation	16	17
Cervical cap (FemCap)	Allergy to spermicide History of TSS Abnormal gynecologic anatomy Abnormal Papanicolaou smear	Latex-free FemCap reusable for up to 2 years	High failure rate Decreased efficacy with parity Cannot be used during menses Cervical irritation	22	22[b]
Spermicides/vaginal pH modulator alone (various nonoxynol-9, lactic acid, citric acid, potassium bitartrate [Phexxi])	Allergy to spermicide/vaginal pH modulator	May provide additional lubrication	High failure rate Must be reapplied before each act of intercourse May increase HIV transmission (nonoxynol-9) No STI protection	16	21[c]
Sponge (Today)	Allergy to spermicide Recurrent UTIs History of TSS Abnormal gynecologic anatomy	Inexpensive	High user failure rate Reduced efficacy with parity Cannot be used during menses No STI protection	12[d]	17[e]

HIV, human immunodeficiency virus; STI/STD, sexually transmitted infection/disease; TSS, toxic shock syndrome; UTI, urinary tract infection.

[a] Failure rate in the United States during the first year of use.

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[b] Failure rate with FemCap reported to be 8% per package insert.

[c] Failure rate with Phexxi reported to be 27.5% per package insert.

[d] Failure rate with Today sponge reported to be 20% in parous individuals.

[e] Failure rate with Today sponge reported to be 29% in parous individuals.

PHARMACOLOGIC THERAPY

Hormonal Contraceptives

- Hormonal contraceptives contain estrogen and progestin or just progestin. They can be administered as oral contraception, transdermal patch, vaginal ring, long-acting injection, subdermal implant, and IUD.
- **Combined hormonal contraceptive** (CHC) contain both estrogen and progestin and work primarily before fertilization to prevent conception.
- Estrogens suppress FSH release, help block the LH surge, stabilize the endometrial lining, and provide cycle control. **Ethinyl estradiol** (EE) is the most common synthetic estrogen; however, estetrol (E4) and estradiol valerate are also used.
- **Progestins** thicken cervical mucus, delay sperm transport, induce endometrial atrophy, block the LH surge, and inhibit ovulation. They vary in progestational activity and differ in estrogenic, antiestrogenic, and androgenic effects. Androgenic activity depends on sex hormone–binding globulin and the androgen-to-progesterone activity ratio. If this globulin decreases, free testosterone levels increase, making androgenic side effects more prominent.
- **Table 80-2** lists available oral contraceptives (OCs) by brand name and hormonal composition.
- Hormonal contraception is typically prescribed, but one formulation is now available over-the-counter. In some states, pharmacists can prescribe self-administered hormonal contraceptives under a state protocol or collaborative agreement.
- With perfect use, CHC efficacy is more than 99%, but with typical use, up to 7% of individuals experience unintended pregnancy. Continuation rates after one year range from 56% to 89%.
- Monophasic CHCs provide a constant amount of estrogen and progestin for 21 days, while biphasic and triphasic pills offer variable amounts. All are followed by a 7-day placebo phase.
- Extended-cycle and continuous combination regimens may reduce adverse effects and are more convenient, with hormone-containing pills increasing from 21 to 84 days. This is followed by a 7-day placebo phase, resulting in four menstrual cycles per year.
- Progestin-only “minipills” are less effective than CHCs and cause irregular menstrual bleeding. They must be taken daily at the same time to remain effective and are linked to more ectopic pregnancies than other hormonal contraceptives.
- The first-day start method begins on the menstrual cycle’s first day. The Sunday start begins the first Sunday after the cycle starts. The quick start method begins on the day of the office visit. A second contraceptive should be used for 7–30 days after CHC initiation, and hormonal contraception should resume no sooner than 5 days after using emergency contraception like ulipristal acetate.
- Provided guidance about what to do if a pill is missed or if vomiting and diarrhea occur.
- CHCs lack protection against STIs, and condoms should be used.
- The choice of an initial CHC is based on hormonal content and dose, preferred formulation, and coexisting medical conditions.
- A complete medical exam and Papanicolaou (Pap) smear aren’t needed before prescribing a CHC. Obtain a medical history, measure blood pressure, and discuss risks, benefits, and adverse effects before prescribing.

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- **Table 80-5** shows graded eligibility criteria for contraceptive use.
- Noncontraceptive benefits of CHCs include fewer menstrual cramps, ovulatory pain, and blood loss; improved menstrual regularity; decreased iron deficiency anemia; and reduced risks of ovarian and endometrial cancer, ovarian cysts, ectopic pregnancy, pelvic inflammatory disease, endometriosis, uterine fibroids, and benign breast disease.

✓ Serious symptoms associated with CHCs are given in **Table 80-3**.

✓ Adverse medication effects occurring in the first cycle of CHC use (eg, breakthrough bleeding, nausea, and bloating) improve by the third cycle of use. **Table 80-4** shows monitoring for CHCs.

✓ Immediately discontinue if any warning signs referred to by the mnemonic ACHES (Abdominal pain, Chest pain, Headaches, Eye problems, and Severe leg pain) occur.

TABLE 80-2

Composition of Commonly Prescribed Oral Contraceptives[a]

Common Brand Names	Estrogen	Micrograms[a] (Number of Days)	Progestin	Milligrams[a] (Number of Days)	Spotting and Breakthrough Bleeding by Third Cycle (Up to Tenth Decimal)
Monophasic Preparations					
Kelnor 1/50	Ethinyl estradiol	50	Ethynodiol diacetate	1	13.9
Zovia 1/35E, Kelnor 1/35	Ethinyl estradiol	35	Ethynodiol diacetate	1	37.4
Apri, Cyred, Cyred EQ, Emoquette, Enskyce, Isibloom, Juleber, Kalliga, Reclipsen	Ethinyl estradiol	30	Desogestrel	0.15	13.1
Azurette, Bekyree, Kariva, Mircette, Pimtrea, Simliya, Viorele, Volnea	Ethinyl estradiol	20 (21) 10 (5)	Desogestrel	0.15	19.7
Nextstellis	Estetrol	14.2 (mg)	Drospirenone	3	N/A
Ocella, Safyral, Syeda, Tydemy, Yasmin, Zarah, Zumandimine	Ethinyl estradiol	30	Drospirenone	3	14.5
Beyaz,[b] Gianvi, Jasmiel, Loryna, Lo-Zumandimine, Nikki, Rajani,[b] Vestura, Yaz[c]	Ethinyl estradiol	20	Drospirenone	3	13.8[d]
Altavera, Ayuna, Chateal, Chateal EQ, Kurvelo, Levora 0.15/30, Marlissa, Portia-28	Ethinyl estradiol	30	Levonorgestrel	0.15	14
Iclevia, Introvale, Jolessa, Setlakin[e]	Ethinyl estradiol	30	Levonorgestrel	0.15	15.1[d]

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Amethia, Ashlyna, Camrese, Daysee, Jaimiess, Seasonique, Simpesse	Ethinyl estradiol	30 (84) 10 (7)	Levonorgestrel	0.15	14.3[f]
Afirmelle, Aubra EQ, Aviane, Balcoltra, Delyla, Falmina, FaLessa, Joyeaux, Larissia, Lessina, Lutera, Orsythia, Sronyx, Tyblume, Vienva	Ethinyl estradiol	20	Levonorgestrel	0.1	26.5
Camrese Lo, LoJaimiess, LoSeasonique	Ethinyl estradiol	20/10	Levonorgestrel	0.1	21.5[f]
Amethyst, Dolishale	Ethinyl estradiol	20	Levonorgestrel	0.09	N/A
Estarylla, Mili, Mono-Linyah, Nymyo, Previfem, Sprintec, VyLibra	Ethinyl estradiol	35	Norgestimate	0.25	14.3
–	Ethinyl estradiol	50	Norgestrel	0.5	N/A
Cryselle, Elinest, Low-Ogestrel, Turqoz	Ethinyl estradiol	30	Norgestrel	0.3	9.6
Balziva, Briellyn, Gildagia, Nexesta Fe chewable, Philith, Vyfemla, Wymzya Fe chewable, Zenchent	Ethinyl estradiol	35	Norethindrone	0.4	11
Necon 0.5/35, Nortrel 0.5/35, Norminest Fe, Wera	Ethinyl estradiol	35	Norethindrone	0.5	24.6
Alyacen 1/35, Cyclafem 1/35, Dasetta 1/35, Nortrel 1/35, Nylia 1/35, Ortho-Novum 1/35, Pirmella 1/35	Ethinyl estradiol	35	Norethindrone	1	14.7
Generess Fe chewable, Kaitlib Fe chewable, Layolis Fe chewable	Ethinyl estradiol	25	Norethindrone	0.8	19.0
Aurovela 1.5/30-21, Aurovela 1.5/30-28, Aurovela Fe 1.5/30, Blisovi Fe 1.5/30, Hailey Fe 1/20, Gildess Fe 1.5/30, Junel 1.5/30, Junel Fe 1.5/30, Larin 1.5/30, Larin Fe 1.5/30, Loestrin Fe 1.5/30, Microgestin 1.5/30, Microgestin Fe 1.5/30	Ethinyl estradiol	30	Norethindrone acetate	1.5	25.2
Aurovela 1/20, Aurovela Fe 1/20, Blisovi 1/20, Hailey Fe 1/20, Junel Fe 1/20, Junel 1/20, Larin (Fe) 1/20, Loestrin 1/20; Fe 1/20, Microgestin 1/20; Microgestin Fe 1/20, Tarina Fe 1/20, Tarina Fe 1/20 EQ	Ethinyl estradiol	20	Norethindrone acetate	1	29.7
Aurovela 24 Fe, Blisovi 24 Fe, Charlotte 24 Fe chewable, Finzala chewable, Gemmily capsules, Junel Fe 24, Hailey 24 Fe, Larin 24 Fe, Minastrin 24 Fe chewable, Merzee capsules, Melodetta 24 Fe chewable, Mibelas 24 Fe chewable, Microgestin 24 Fe, Tarina 24 Fe, Taytulla capsules	Ethinyl estradiol	20	Norethindrone acetate	1	23.2[d]
Lo Loestrin-24 Fe[c]	Ethinyl	10	Norethindrone	1	52.0[d]

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	estradiol		acetate		
Multiphasic Preparations (Biphasic, Triphasic, and Quadriphasic)					
–	Ethinyl estradiol	35 (10) 35 (11)	Norethindrone	0.5 (10) 1 (11)	N/A
Caziant, Cyclessa, Velivet	Ethinyl estradiol	25 (7) 25 (7) 25 (7)	Desogestrel	0.1 (7) 0.125 (7) 0.15 (7)	11.1
Enpresse, Trivora, Levonest Myzilra	Ethinyl estradiol	30 (6) 40 (5) 30 (10)	Levonorgestrel	0.05 (6) 0.075 (5) 0.125 (10)	15.1
Tri-Estarylla, Tri-Linyah, Tri-Mili, Tri-Nymyo, TriNessa, Tri-Previfem, Tri-Sprintec, Tri-VyLibra	Ethinyl estradiol	35 (7) 35 (7) 35 (7)	Norgestimate	0.18 (7) 0.215 (7) 0.25 (7)	17.7
Ortho-Tri Cyclen Lo, Tri-Lo Estarylla, Tri-Lo-Marzia, Tri-Lo-Mili, Tri-Lo-Sprintec, Tri-VyLibra Lo	Ethinyl estradiol	25 (7) 25 (7) 25 (7)	Norgestimate	0.18 (7) 0.215 (7) 0.25 (7)	11.5
Alyacen 7/7/7, Cyclafem 7/7/7, Dasetta 7/7/7, Nortrel 7/7/7, Nylia 7/7/7, Ortho Novum 7/7/7/, Pirmella 7/7/7	Ethinyl estradiol	35 (7) 35 (7) 35 (7)	Norethindrone	0.5 (7) 0.75 (7) 1 (7)	14.5
Aranelle, Leena	Ethinyl estradiol	35 (7) 35 (9) 35 (5)	Norethindrone	0.5 (7) 1 (9) 0.5 (5)	25.5
Estrostep Fe, Tilia Fe, Tri-Legest Fe	Ethinyl estradiol	20 (5) 30 (7) 35 (9)	Norethindrone acetate	1 (5) 1 (7) 1 (9)	21.7
Fayosim, Quartette, Rivelsa	Ethinyl estradiol	20 (42)	Levonorgestrel	0.15	N/A

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		25 (21)			
		30 (21)			
		10 (7)			
Natazia	Estradiol valerate	3 (2)	Dienogest	0 (2)	14
		2 (5)		2 (5)	
		2 (17)		3 (17)	
		1 (2)		0 (4)	
Progestin-Only Oral Contraceptives					
Camila, Deblitane, Errin, Heather, Incassia, Jencycla, Lyleq, Lyza, Ortho Micronor, Nora-BE, Norlyda, Norlyroc, Sharobel, Tulana	Ethinyl estradiol	–	Norethindrone	0.35 (28)	42.3
Opill	Ethinyl estradiol	_	Norgestrel	0.075 (28)	N/A
Slynd	Ethinyl estradiol	–	Drospirenone	4 (24)	N/A

N/A—data not available per references.

[a]28-day regimens (21-day active pills, then 7-day pill-free interval) unless otherwise noted.

[b]Also contains levomefolate calcium 0.451 mg in all 28 tablets.

[c]Number in parentheses refers to the number of days the dose is received in multiphasic oral contraceptives.

[d]28-day regimen (24-day active pills, then 4-day pill-free interval).

[e]91-day regimen (84-day active pills, then 7-day pill-free interval).

[f]Percent reporting after 6 to 12 months of use.

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TABLE 80-3

Serious or Potentially Serious Symptoms Associated with Combined Hormonal Contraception

Serious: Stop Immediately	
Loss of vision, proptosis, diplopia, papilledema Unilateral numbness, weakness, or tingling Severe pain in chest, left arm, or neck	Hemoptysis Severe pain, tenderness or swelling, warmth or palpable cord in legs Hepatic mass or tenderness Slurring of speech
Potentially Serious: May Continue with Caution While Being Evaluated	
Absence of menses Spotting or breakthrough bleeding Breast mass, pain, or swelling Right upper-quadrant pain Mid-epigastric pain Migraine headache	Severe nonvascular headache Galactorrhea Jaundice, pruritus Depression, sleepiness Uterine size increase

TABLE 80-4

Monitoring for Hormonal Contraception

Adverse Medication Effect	Monitoring Parameter	Comments
Combined Hormonal Contraception		
Nausea/vomiting Breast tenderness Weight gain	Patient symptoms and weight	Typically improves after two to three cycles; consider changing to lower estrogenic
Acne, oily skin	Visual inspection	Consider changing to lower androgenic
Depression, fatigue	Depression screening	Data are limited and conflicting
Breakthrough bleeding/spotting	Menstrual symptoms	Consider changing to higher estrogenic
Application site reaction (transdermal)	Visual inspection	
Vaginal irritation (vaginal ring)	Patient symptoms	
Depot Medroxyprogesterone Acetate		
Menstrual irregularities[a]	Menstrual symptoms	Typically improves after 6 months

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Weight gain Acne Hirsutism Depression	Weight, visual inspection, and depression screening	Data are limited and conflicting
Decreased bone density	Bone mineral density (BMD)	Do not routinely screen with dual-energy X-ray absorptiometry (DXA)
Levonorgestrel and Copper IUD		
Menstrual irregularities[a]	Menstrual symptoms	Typically spotting, amenorrhea Typically heavier menses with copper IUD
Insertion-related complications	Cramping, pain	Prophylactic nonsteroidal anti-inflammatory drugs (NSAIDs) or local anesthetic may reduce occurrence
Expulsion	Cramping, pain, spotting, dyspareunia, missing strings	IUD strings should be checked regularly to ensure IUD properly placed
Pelvic inflammatory disease	Lower abdominal pain, unusual vaginal discharge, fever	Overall risk of developing is rare, but counseling on STI prevention is important
Progestin-Only Implant		
Menstrual irregularities[a]	Menstrual symptoms	Typically well-tolerated and resolve without treatment; infection is rare
Insertion-site reactions	Pain, bruising, skin irritation, erythema, pus, fever	

[a] Suggested management of irregular bleeding may include use of NSAIDs for 5–7 days; hormonal treatment (if medically eligible) with CHC or estrogen therapy for 10–20 days of treatment.

TABLE 80-5

US Medical Eligibility Criteria for Contraceptive Use: Classifications for Combined Hormonal Contraceptives

Category 4: Unacceptable Health Risk (method not to be used) • Breastfeeding or nonbreastfeeding <21 days postpartum • Current breast cancer • Severe (decompensated) cirrhosis • Current DVT/PE • History/higher risk of DVT/PE (not on anticoagulant therapy) • History/higher risk of DVT/PE (established on anticoagulant therapy for 3 months or greater) • Thrombogenic mutations • Major surgery with prolonged immobilization • Migraines with aura, any age • Systolic BP ≥160 mm Hg or diastolic ≥100 mm Hg • Hypertension with vascular disease • Current and history of ischemic heart disease • Benign hepatocellular adenoma or malignant liver tumor	• Diabetes mellitus (type 1 or type 2), nonvascular disease • Gallbladder disease; symptomatic and treated by cholecystectomy or asymptomatic • Migraines without aura • History of pregnancy-related cholestasis • History of high BP during pregnancy • Benign liver tumors; focal nodular hyperplasia • BMI ≥30 kg/m^2 (Obesity) • Breastfeeding 30-42 days postpartum without other VTE risk factors • Breastfeeding 42 days or more postpartum • Nonbreastfeeding 21–42 days postpartum without other risk factors for VTE • Rheumatoid arthritis on or off

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- Peripartum cardiomyopathy, moderately or severely impaired cardiac function; normal or mildly impaired cardiac function <6 months
- Smoking ≥15 cigarettes per day and age ≥35
- Complicated solid organ transplantation, graft failure
- History of cerebrovascular accident
- SLE; positive or unknown antiphospholipid antibodies
- Current nephrotic syndrome
- Hemodialysis
- Peritoneal dialysis
- Sickle cell disease
- Complicated valvular heart disease

Category 3: Theoretical or Proven Risks Usually Outweigh the Advantages

- Breastfeeding 21-30 days postpartum with or without risk factors for VTE
- Breastfeeding 30-42 days postpartum with other risk factors for VTE
- Nonbreastfeeding 21-42 days postpartum with other risk factors for VTE
- Past breast cancer and no evidence of disease for 5 years
- History of DVT/PE (not on anticoagulant therapy or established on anticoagulant therapy for at least 3 months), but lower risk for recurrent DVT/PE
- Current gallbladder disease, symptomatic and medically treated
- History of bariatric surgery; malabsorptive procedures (*COCs only, vaginal ring/transdermal patch category 1*)
- History of cholestasis, past COC-related
- Hypertension; systolic BP 140–159 mm Hg or diastolic 90–99 mm Hg
- Adequately controlled hypertension
- Peripartum cardiomyopathy, normal or mildly impaired cardiac function ≥6 months
- Smoking <15 cigarettes per day and age ≥35
- Use of fosamprenavir
- Use of certain antiseizure medications (phenytoin, carbamazepine, barbiturates, primidone, topiramate, oxcarbazepine, and lamotrigine)
- Use of rifampicin or rifabutin therapy
- Diabetes with vascular disease or >20 years duration (*possibly category 4 depending upon severity*)
- Multiple risk factors for arterial cardiovascular disease (older age, smoking, diabetes, low HDL, high LDL, or high triglycerides and hypertension) (*possibly category 4 depending on category and severity*)
- Acute flare of viral hepatitis (*possibly category 4 depending on severity [initiation]*)
- Multiple sclerosis with prolonged immobility
- Current or history of superficial venous thrombosis

Category 2: Advantages Generally Outweigh Theoretical or Proven Risks

- Age ≥40 (in the absence of other comorbid conditions that increase CVD risk)
- Undiagnosed breast mass
- Cervical cancer and awaiting treatment; cervical intraepithelial neoplasia
- Family history (first-degree relatives) of DVT/PE
- Major surgery without prolonged immobilization
- Use of immunosuppressive therapy
- Smoking and <35 years old
- Uncomplicated solid organ transplantation, graft failure
- SLE with severe thrombocytopenia or on immunosuppressive therapy or without antiphospholipid antibodies
- Unexplained vaginal bleeding before evaluation
- Uncomplicated valvular heart disease
- Use of antiretrovirals other than fosamprenavir (*category 1 or 2 depending on agent*)
- Use of St. John's wort
- Inflammatory bowel disease (*possibly category 3 for those with increased risk of VTE*)
- Acute flare of viral hepatitis occurring during use of product (*continuation, category 3 or 4 for initiation of product*)

Category 1: No Restriction (method can be used)

- Thalassemia, iron deficiency anemia
- Mild compensated cirrhosis
- Benign ovarian tumors
- Benign breast disease or family history of cancer
- Family history of cancer
- Schistosomiasis
- Cystic fibrosis
- Cervical ectropion
- Viral hepatitis (carrier/chronic)
- Minor surgery without immobilization
- Depression
- Gestational diabetes mellitus
- Endometrial cancer/hyperplasia, endometriosis
- Epilepsy
- Gestational trophoblastic disease
- Nonmigrainous headaches
- History of bariatric surgery; restrictive procedures
- History of pelvic surgery
- HIV infected or high risk
- Malaria
- Multiple sclerosis without prolonged immobility
- Ovarian cancer
- Past ectopic pregnancy
- Parity, parous, or nulliparous
- PID
- Postabortion
- Nonbreastfeeding more than 42 days postpartum
- Severe dysmenorrhea
- STIs

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	• Varicose veins • Vaginal bleeding—irregular pattern without heavy bleeding or heavy, prolonged bleeding • Thyroid disorders • Tuberculosis • Uterine fibroids • Use of SSRIs • Use of broad-spectrum antibiotics, antifungals, and antiparasitics

CVD, cardiovascular disease; DVT, deep vein thrombosis; HDL, high-density lipoprotein; LDL, low-density lipoprotein; PE, pulmonary embolism; PID, pelvic inflammatory disease; SSRI, selective serotonin reuptake inhibitors.

Transdermal Contraceptives

- Two combination contraceptives are available as **transdermal patches**. Xulane delivers 35 mcg EE and 150 mcg norgestimate daily, while Twirla provides 120 mcg levonorgestrel and 30 mcg EE daily. They are effective as CHCs for individuals weighing less than 90 kg (198 lb) or with a BMI under 30 kg/m^2, having failure rates between 3% and 7%.

  ✓ Apply the patch to the abdomen, buttocks, upper torso, or upper arm at the start of the menstrual cycle and replace it weekly for 3 weeks, followed by a patch-free fourth week. Individuals should be counseled on steps to take if the patch detaches or is forgotten.

  ✓ Approved labeling includes a warning regarding VTE risk.

Vaginal Rings

- Two vaginal rings are available: **NuvaRing** releases about 15 mcg/day of EE and 120 mcg/day of etonogestrel over 3 weeks, while **Annovera** releases 13 mcg of EE and 150 mcg of segesterone acetate. Insert the ring by the fifth day of the cycle, keep it in for 3 weeks, then remove it for 1 week. Insert a new ring on the same weekday as the previous cycle. Use a second contraceptive for the first 7 days of use or if NuvaRing is expelled for over 3 hours or Annovera for over 2 hours.

- If Annovera is not removed after 4 weeks, no backup is needed, but wait 1 week before inserting a new ring. Annovera can be used for 13 cycles and doesn't need refrigeration. If NuvaRing stays in place for 4 weeks, take a pregnancy test and use a new ring with 7 days of nonhormonal contraception.

Injectable Progestins

- Progestin-only methods, like minipills, benefit individuals who are lactating, intolerant to estrogens, or have medical conditions where estrogen is not recommended (**Table 80-3**).

- Injectable and implantable contraceptives are also beneficial for individuals with adherence issues as failure rates are lower than with CHC.

- **Depot medroxyprogesterone acetate (DMPA)** 150 mg is injected intramuscularly in the gluteal or deltoid muscle within 5 days of menstrual onset and repeated every 12 weeks. A 104-mg formulation (Depo-SubQ Provera 104) is injected subcutaneously into the thigh or abdomen. Exclude pregnancy if more than 1 week late for the intramuscular injection or 2 weeks late for the subcutaneous one. Fertility return may be delayed after stopping.

- DMPA can be given immediately postpartum for nonbreastfeeding individuals and at 6 weeks postpartum if breastfeeding. Median time to conception after the first missed dose is 10 months.

  ✓ DMPA is contraindicated with a current breast cancer diagnosis and used cautiously with a history of breast cancer, cardiovascular

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disease, or lupus.

✓ The most common adverse effect is menstrual irregularity, which decreases after the first year. Breast tenderness, weight gain, and depression are less frequent.

✓ DMPA carries a black box warning for reduced bone mineral density (BMD) but not an increased fracture risk. BMD loss tends to increase with longer use but is usually reversible. DMPA should not be used beyond 2 years unless other contraceptives are inadequate.

Subdermal Progestin Implants

- **Etonogestrel implant**: Nexplanon is a radiopaque, 4-cm implant with 68 mg of etonogestrel, placed under the skin in the upper arm. It releases 60 mcg daily initially, decreasing to 30 mcg/day by the end of 3 years. Efficacy exceeds 99% but may be lower in those over 130% of ideal body weight.
- Its contraceptive effects are quickly reversible upon removal.
- Backup contraception needs depend on previous contraceptive use and timing of implant insertion in the menstrual cycle. Fertility returns 30 days after removal.

  ✓ Irregular menstrual bleeding is common, followed by headache, vaginitis, weight gain, acne, and breast and abdominal pain. It doesn't seem to decrease BMD.

  ✓ There is potential for interactions in the presence of potent CYP450 inducers (eg, rifampin, phenytoin, and carbamazepine).

Intrauterine Devices (IUDs)

- Contraceptive activity occurs before implantation. Progestin-releasing IUDs cause endometrial suppression. Efficacy exceeds 99%, and effects are reversible upon removal.
- IUDs are suitable for nulliparous and adolescent individuals due to high efficacy and low complication rates. Backup contraception needs depend on prior use and timing of insertion within the menstrual cycle.
- The risk of pelvic inflammatory disease among users is low with no long-term effects on fertility.
- ParaGard (copper) can remain for 10 years. Mirena and Liletta must be replaced after 6 years, Kyleena after 5 years, and Skyla after 3 years, as they release levonorgestrel.

  ✓ ParaGard may cause increased menstrual blood flow and dysmenorrhea. Levonorgestrel IUDs often reduce menstrual blood loss and may cause amenorrhea.

Special Consideration for Contraceptive Use

Smoking

- CHCs with less than 50 mcg estrogen can be used by healthy nonsmokers over 35. They aren't recommended for those over 35 with migraines, uncontrolled hypertension, smoking, or diabetes with vascular issues.
- Studies show no increased cardiovascular risk with low-dose CHCs in healthy, nonobese individuals.
- Smoking 15+ cigarettes daily for those over 35 is a contraindication for CHCs; progestin-only methods are advised.

Hypertension

- CHCs can slightly increase blood pressure (6–8 mm Hg). Avoid CHCs if systolic pressure is 140–159 or diastolic is 90–99. They are contraindicated at pressures ≥160/100 mm Hg.

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- Low-dose CHCs are acceptable for those under 35 with well-controlled, monitored hypertension to lower MI and stroke risk.
- Monitor potassium if using potassium-sparing diuretics, ACE inhibitors, angiotensin-receptor blockers, or aldosterone antagonists with drospirenone-containing products.

Diabetes

- Nonsmoking individuals under 35 with diabetes but no vascular disease can safely use CHCs. Those with diabetes for over 20 years or with vascular disease should avoid CHCs.

Dyslipidemia

- Generally, synthetic progestins decrease high-density lipoprotein (HDL) and increase low-density lipoprotein (LDL), while estrogens decrease LDL and increase HDL, potentially raising triglycerides.
- Most low-dose CHCs don't significantly affect HDL, LDL, triglycerides, or cholesterol. The increased cardiovascular risk in CHC users is linked to thromboembolic changes, not atherosclerosis.
- CHCs are acceptable for those with dyslipidemia as a single risk factor but are not recommended if there are additional cardiovascular risk factors.

Thromboembolism

- The risk of venous thromboembolism (VTE) is three times higher in combined oral contraceptive (COC) users than nonusers, but lower than during pregnancy.
- Estrogens elevate hepatic production of coagulation factors. Thromboembolic risk increases with hypercoagulable states or conditions like obesity, pregnancy, immobility, trauma, surgery, and certain cancers that predispose to coagulation abnormalities.
- COCs with newer progestins like drospirenone, desogestrel, and norgestimate slightly increase thrombosis risk compared to older progestins for unknown reasons.
- The transdermal patch and vaginal ring have higher continuous estrogen exposure, increasing thromboembolic risk.
- For those over 35 or at higher thromboembolism risk due to obesity, smoking, history of thrombosis, or prolonged immobilization, consider low-dose oral estrogens with older progestins or progestin-only methods.

Obesity

- COCs are less effective in obese individuals, with low-dose versions being more problematic. IUDs, implants, and DMPA have low failure rates and are safe for obese individuals.
- Obesity increases VTE risk; progestin-only contraception may be preferable for those over 35.

Migraine Headache

- CHCs can alter migraine frequency. They may be suitable for healthy, nonsmoking individuals under 35 with migraines without aura. Discuss risks and benefits with those developing migraines without aura.
- CHCs are not for anyone with migraines with aura due to stroke risk; those developing aura migraines on CHCs should stop use and consider progestin-only options.

Breast Cancer

- CHCs slightly increase breast cancer risk while taken and for 5–10 years after stopping. Alternatives may be better for those over 40 or with

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elevated breast cancer risk. Benign breast disease or family history shouldn't influence CHC use.

- CHC use is controversial for BRCA1 or BRCA2 mutations, and those with current or past breast cancer should avoid CHCs.

Systemic Lupus Erythematosus (SLE)

- COCs with under 50 mcg EE do not increase flare risk in stable SLE without antiphospholipid/anticardiolipin antibodies.
- Avoid CHCs and progestin-only products in SLE with antiphospholipid antibodies or vascular issues; consider the copper IUD.
- For SLE without these complications, progestin-only contraceptives or the copper IUD are alternatives.
- Avoid copper IUDs and DMPA in SLE with severe thrombocytopenia.

Postpartum

- Avoid estrogen-containing contraceptives in the first 21 days postpartum due to increased VTE risk; use progestin-only products if needed.
- Avoid CHCs for 42 days postpartum with VTE risk factors and 30 days for breastfeeding individuals without such factors.

Medication Interactions

- Advise patients to use alternative contraception if a medication interaction may affect OC efficacy.
- There is a small interaction risk with antimicrobials; consider additional nonhormonal methods, especially if using antimicrobials for over 2 months.
- Rifampin reduces CHC efficacy; use additional nonhormonal contraception for at least 7–28 days after therapy. Phenobarbital, carbamazepine, and phenytoin may also reduce CHC efficacy, and many anticonvulsants are teratogens. Consider IUDs, injectable medroxyprogesterone, or nonhormonal options.
- CHCs can decrease lamotrigine efficacy, raising seizure risk. Some antiretrovirals and St. John's wort may also reduce CHC efficacy.
- Monitor potassium in patients using drospirenone with medications that increase potassium or strong CYP3A4 inhibitors.
- Oral progestin-only tablets, especially norethindrone and norgestrel, may have interactions as they're metabolized via the cytochrome P450 system.

Return of Fertility After Discontinuation

- There is no evidence that hormonal contraception use decreases subsequent fertility and there is no greater chance of miscarriage or a birth defect in the first month after discontinuation.

Emergency Contraception (EC)

- EC prevents pregnancy after unprotected or inadequately protected intercourse.
- FDA-approved progestin-only and progesterone receptor modulators are first-line options and won't affect implantation if it has occurred.
- Progestin-only EC with 1.5-mg levonorgestrel is OTC in the United States, but may be less effective in individuals weighing greater than 75 kg.
- **Ulipristal** (Ella) a prescription progesterone modulator, is taken as a 30-mg dose within 120 hours of unprotected sex. It is noninferior to levonorgestrel EC but not recommended for breastfeeding individuals.
- Common EC side effects include nausea, vomiting, and irregular bleeding.

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- Copper IUD insertion or higher-dose CHCs (Yuzpe method) are alternative EC options.
- EC should be taken within 72 hours of unprotected sex; earlier use improves efficacy. Ulipristal or a copper IUD may be more effective if used within 5 days.
- Backup nonhormonal contraceptive methods should be used after EC for at least 7 days.

Pregnancy Termination

- For early pregnancy termination (≤70 days), **mifepristone** and **misoprostol** are used. Misoprostol is more effective with mifepristone. The FDA-approved regimen is mifepristone 200 mg orally on day 1, followed by misoprostol 800 mcg buccally 24–48 hours later, with 98% efficacy up to 49 days.
- Mifepristone blocks progesterone, softening the cervix and increasing prostaglandin sensitivity, leading to contractions. It is taken orally and provided under the REMS program by certified prescribers and pharmacies. It is contraindicated for those with bleeding disorders or on anticoagulants, and as a CYP3A4 substrate, medication interactions must be considered.
- Misoprostol, a prostaglandin 1 analog, is well absorbed vaginally, buccally, or sublingually, causing cervical ripening and contractions. Oral use is not recommended.

  ✓ Misoprostol can cause upset stomach, diarrhea, headache, dizziness, and fever. Mifepristone's boxed warning includes infection and excessive bleeding, which may indicate complications and requires immediate medical attention

EVALUATION OF THERAPEUTIC OUTCOMES

- Annually monitor blood pressure in CHC users and closely check glucose when starting or stopping CHCs in those with diabetes or glucose intolerance.
- Conduct annual exams for contraceptive users, including screenings and evaluating issues like bleeding, amenorrhea, weight gain, and acne; these aren't required before prescribing.
- Annually monitor Nexplanon users for menstrual changes, weight, implant site reactions, acne, breast tenderness, headaches, and hair loss.
- Evaluate DMPA users every 3 months for weight, menstrual changes, and fractures.
- Check IUD users every 1–3 months for positioning, menstrual changes, and upper genital tract infections.
- Clinicians should screen for HIV/STIs as indicated and advise on safe sexual practices, including condom use to prevent STIs.

See Chapter 104, Contraception, authored by Shareen Y. El-Ibiary, for a more detailed discussion of this topic.

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